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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/206,249	12/07/1998	MIRI SEIBERG	JBP438	5255

7590 05/04/2010

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EXAMINER	
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ART UNIT	PAPER NUMBER
1655	

MAIL DATE	DELIVERY MODE
05/04/2010	PAPER

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MIRI SEIBERG, STANLEY S. SHAPIRO,
and MAGDALENA G. EISINGER

Appeal 2009-013439
Application 09/206,249
Technology Center 1600

Decided: May 4, 2010

Before CAROL A. SPIEGEL, TONI R. SCHEINER, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to methods for topically applying a non-denatured soy extract having active trypsin inhibitory activity. We have jurisdiction under 35 U.S.C. § 6(b). We affirm and denominate our affirmance as a NEW GROUND OF REJECTION.

Statement of the Case

The Claims

Claims 75-84 are on appeal. Claims 75 is representative and reads as follows:

> 75. A topical method of decreasing phagocytosis or ICAM-1 expression in a patient having one or more of the conditions consisting of pulmonary emphysema, immunological lung disorders, periodontal disease, atherosclerotic plaques, Mid-dermal elastosis, pigmentation disorders, psoriasis, eczema and Acne vulgaris, comprising applying topically to an affected organ of said patient a therapeutically phagocytosis- or ICAM-1 decreasing effective amount of composition containing active trypsin inhibitory activity comprising a non-denatured soy extract having active trypsin inhibitory activity.

The prior art

The Examiner relies on the following prior art reference to show unpatentability:

Matsuura et al. JP 408143442[1] Jun. 4, 1996

The issue[2]

The Examiner rejected claims 75-84 under 35 U.S.C. § 102(b) as anticipated by Matsuura (Final Rej[3]. 3-4).

The Examiner finds that Matsuura "teaches a water extract of soybeans used to treat eczema. Whole soybeans are ground and water is

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[1] This decision cites to the translation of record supplied by Appellants.
[2] The Examiner withdrew an anticipation rejection over JP 410226642 (*see* Ans. 3).
[3] We refer to the Final Rejection mailed March 20, 2008.

added and then the extract is filtered. The ground matter is heated but to a temperature which could read on 5°C" (Final Rej. 3).

Appellants argue that "in view of the Declaration of Miri Seiberg dated July 30, 2008 and attached hereto in the Exhibit Appendix, the soybean extract of JP '442 would *not necessarily* contain STI [soy trypsin inhibitors]" (App. Br. 6). Appellants also "contend that one of ordinary skill in the art following Matsuura would, therefore, not *necessarily* obtain a soybean extract that contains non-denatured soy trypsin inhibitory activity" (App. Br. 6).

In view of these conflicting positions, we frame the anticipation issue before us as follows:

Does the evidence support the Examiner's finding that Matsuura's soybean extract inherently contains trypsin inhibitory activity?

Findings of Fact (FF)

1. The Specification teaches that "[n]atural compounds that inhibit trypsin, such as serine protease inhibitors, and in particular, soybean trypsin inhibitor ('STI'), can be used for this invention" (Spec. 16, ll. 12-15).

2. The Specification teaches that "[s]oybean extracts, limabean extracts and similar extracts, and other natural products made from soybean and the like, such as soybean milk, soybean paste, miso, trypsin inhibitor from soybean or limabean and the like, can also reduce phagocytosis by this mechanism" (Spec. 16, ll. 15-20).

3. The Specification teaches that in "the preferred embodiment, the naturally occurring composition is soy milk or STI" (Spec. 16, ll. 20-21).

4. Matsuura teaches an "external preparation for skin comprising a water extract liquid of soybeans" (Matsuura Trans. 2, claim 1).

5. Matsuura teaches:

> A process for producing an external preparation for skin characterized by soaking whole soybeans, dehulled soybeans or defatted soybeans in water at 5 to 100ºC for 5 minutes to 20 hours, removing soybeans, to the obtained soaked liquid as such or after it is concentrated, adding any of a variety of bases, fragrances, colorants and the like and mixing them.

(Matsuura Trans. 2-3, claim 5).

6. Matsuura teaches that "in order to prevent the elution of proteins as much as possible, the pH of water for soaking during soaking is preferably adjusted at 4 to 5 with an organic acid or an inorganic acid", "where a soaked liquid of defatted soybeans is used as a raw material" (Matsuura Trans. 7, ¶ 9).

7. Matsuura teaches in Example 1 that:

> Whole soybeans were heated with hot air at 75°C, and then pressed and dehulled with a roller. Then, hulls and embryonic axes were removed, whereby dehulled soybeans each of which was divided into two pieces were obtained. These dehulled soybeans were ground while adding 10 times volume of cold water (5°C) thereby to obtain mashed soybeans.

(Matsuura Trans. 9, ¶ 12).

8. Matsuura teaches in Example 1 that the "resulting mashed soybeans were heated at 100°C for 30 seconds, and then cooled to 80°C, and solid-liquid separation was carried out using a screw decanter, whereby soymilk was obtained" (Matsuura Trans. 9, ¶ 12).

9. Matsuura teaches in Example 1 that the "obtained soymilk was degassed, and thermal sterilization at 120°C for 3 minutes was carried out. Then, the concentration of proteins was adjusted to 3.5%" (Matsuura Trans. 9, ¶ 12).

10. Matsuura teaches in Example 1 that "the soymilk was filtered with an ultrafiltration membrane having a fractionation molecular weight of 300,000, and a low molecular weight fraction was collected as a filtrate" (Matsuura Trans. 9, ¶ 12).

11. Matsuura teaches in Example 1 that this "filtrate was concentrated . . . and an ointment base . . . was mixed with this concentrated liquid at a ratio of 8 to 2 (ointment base : concentrated liquid), whereby a skin application agent (ointment) was obtained" (Matsuura Trans. 9-10, ¶ 13).

12. Matsuura teaches in Example 1 that "[s]ubjects who had the symptoms shown in Table 2 were allowed to use the above-mentioned ointment by applying it on the affected area three times daily and the conditions after the use were examined through interviews" (Matsuura Trans. 10, ¶ 14).

13. Matsuura teaches in Example 1 that the ointment was applied to a "subject in his 40's (male). Symptoms: Atopic eczema appeared on the legs and there was itching. After use: The itching disappeared right after the application thereof. The affected area dried out and the brown color of the skin of the affected area became lighter" (Matsuura Trans. 12, ¶ 19).

14. Van der Ven[4] teaches that "[d]ehulled soybeans . . . were soaked overnight in demineralized water at 5 °C (w/v = 1:5). Some soaked beans were removed and stored for high-pressure treatment. The remaining soybeans were ground in a blender with the soaking water to soy milk. The pulp was removed by filtration over a nylon cloth" (Van der Ven 1088).

15. Van der Ven teaches that "[r]eported conditions for heat inactivation of TIA [trypsin inhibitor] are, for example, 30 min at 100 °C or 22 min at 110 °C (*9*)" (Van der Ven 1091, col. 1).

16. Van der Ven teaches that for "UHT [ultrahigh temperature] inactivation, 143 °C and 62 s are needed to reach 90% TIA inactivation, whereas for temperatures lower than ~ 136 °C, 90% inactivation within 90 s of treatment time (the maximum treatment time tested) was not possible" (Van der Ven 1091, col. 1).

17. Kwok[5] teaches that:

> Due to the necessity of achieving a balance between the heat necessary to destroy the trypsin inhibitors and that which can potentially damage the nutritional value or functional properties of the protein, most commercially available edible-grade soybean products actually retain 5−20% of the TIA present in the original raw soybean from which they were prepared (*16*). The extent of destruction of TIA in soy milk for maximum nutritive value or protein efficiency ratio was reported to be 90%.

(Kwok 4836, col. 2).

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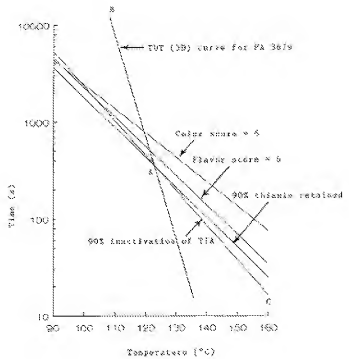
[4] Van der Ven et al., *Inactivation of Soybean Trypsin Inhibitors and Lipoxygenase by High-Pressure Processing*, 53 J. AGRIC. FOOD CHEM. 1087-1092 (2005).

[5] Kwok et al., *Optimizing Conditions for Thermal Processes of Soy Milk*, 50 J. AGRIC. FOOD CHEM. 4834-4838 (2002).

18. Figure 1 of Kwok is reproduced below:



"Figure 1. Relationship between heating time and temperature in soy milk processing for . . . 90% inactivation of TIA" (Kwok 4836, col. 2).

19. Figure 1 of Kwok shows that at 120°C, 90% inactivation of trypsin inhibitor activity occurs after more than 400 seconds, or more than 6 ½ minutes (*see* Kwok, Figure 1, FF 16).

Principles of Law

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987).

"It is well settled that a prior art reference may anticipate when the claim limitations not expressly found in that reference are nonetheless inherent in it." *In re Cruciferous Sprout Litigation*, 301 F.3d 1343, 1349

(Fed. Cir. 2002). *See, e.g., MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365 (Fed.Cir.1999) ("Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates.")

Once a prima facie case of anticipation has been established, the burden shifts to the Appellant to prove that the prior art product does not necessarily or inherently possess the characteristics of the claimed product. *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) ("Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product."). *See also In re Spada*, 911 F.2d 705, 708-09 (Fed. Cir. 1990).

Analysis

Matsuura teaches, in Example 1, a method of preparation of an ointment where whole soybeans are first made into soymilk which involves mashed soybeans that were heated to 100°C for 30 seconds, and cooled to 80°C (FF 7-9). Matsuura teaches in Example 1 that the "obtained soymilk was degassed, and thermal sterilization at 120°C for 3 minutes was carried out. Then, the concentration of proteins was adjusted to 3.5%" (Matsuura Trans. 9; FF 10). Matsuura filters this soymilk and then forms an ointment with the filtrate (FF 11). Matsuura teaches that a patient with eczema applied the ointment to his skin (FF 12-13).

Appellants argue that "in view of the Declaration of Miri Seiberg dated July 30, 2008 and attached hereto in the Exhibit Appendix, the

soybean extract of JP '442 would *not necessarily* contain STI" (App. Br. 6). Dr. Seiberg states that "[i]t is obvious to those of ordinary skill in the art from this diffusion coefficient that STI will not diffuse out of the soybean into any soaking liquid" (Seiberg Dec. 7/30/08 ¶ 7).

Appellants argue that "Matsuura indicates that the soaked soybean material is subjected to high heat, i.e., 80-100°C and then sterilized at 120°C" (App. Br. 6). Appellants point to the Zivin Declaration that high heat may deactivate proteins and argue that "one of ordinary skill in the art following Matsuura would . . .not *necessarily* obtain a soybean extract that contains non-denatured soy trypsin inhibitory activity" (App. Br. 6).

We are not persuaded. Appellants' Specification states that a preferred source for soybean trypsin inhibitors is soy milk (FF 1-3), and Matsuura teaches and exemplifies the use of an ointment which contains filtered and concentrated soy milk for treatment of eczema (FF 4-13). Example 1 of Matsuura does not use any denaturing solvents, but rather only adds water to the soybeans (FF 7). Appellants have not demonstrated that the temperatures used by Matsuura differ from those normally used to prepare soy milk.

However, in the interest of ensuring accuracy in the inherency determination, we have identified two references,[6] Kwok and Van der Ven. A review of their data provides evidence to support the inherent anticipation of Example 1 of Matsuura. Due to the introduction of these additional

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[6] While these references are post-filing date, we note that "recognition by a person of ordinary skill in the art before the critical date of the . . . patent is not required to show anticipation by inherency." *Schering Corp. v. Geneva Pharmaceuticals*, 339 F.3d 1373, 1377 (Fed. Cir. 2003).

references, we denominate the anticipation rejection over Matsuura as a New Ground of Rejection.

Both Kwok and Van der Ven teach that soymilk contains trypsin inhibitor activity (FF 14-19). Van der Ven obtains the soymilk using a process similar to that of Matsuura, in which soybeans are soaked in water, mashed, and the resulting liquid soymilk is filtered (*see* FF 7-8, 14). Kwok teaches that "most commercially available edible-grade soybean products actually retain 5–20% of the TIA present in the original raw soybean from which they were prepared (*16*). The extent of destruction of TIA in soy milk for maximum nutritive value or protein efficiency ratio was reported to be 90%" (Kwok 4836, col. 2; FF 17).

Therefore, Van der Ven and Kwok directly rebut Dr. Seiberg's testimony that "STI will not diffuse out of the soybean into any soaking liquid" (Seiberg Dec. 7/30/08 ¶ 7). Van der Ven demonstrates soybean trypsin inhibitor eluted from soybeans into soymilk and Kwok also states that soymilk contains soybean trypsin inhibitor (FF 14, 17).

Both Kwok and Van der Ven also address the temperature sensitivity of soybean trypsin inhibitor to high temperatures. Van der Ven teaches that "[r]eported conditions for heat inactivation of TIA are, for example, 30 min at 100 °C or 22 min at 110 °C (*9*)" (Van der Ven 1091, col. 1; FF 15). Van der Ven also teaches that for "UHT inactivation, 143 °C and 62 s are needed to reach 90% TIA inactivation, whereas for temperatures lower than ~ 136 °C, 90% inactivation within 90 s of treatment time (the maximum treatment time tested) was not possible" (Van der Ven 1091, col. 1; FF 16).

Kwok provides Figure 1 which shows that at 120°C, 90% inactivation of trypsin inhibitor activity occurs after more than 400 seconds, or more than 6 ½ minutes (FF 18-19). Thus, based upon the teachings of Kwok and Van der Ven, the 120°C heat treatment for 3 minutes of Matsuura would not have reasonably been expected to reach 90% inactivation, leaving more than 10% of the original soybean trypsin inhibitor activity as present in the finished ointment, which was used by Matsuura to treat a patient with eczema (FF 13).

Conclusion of Law

The evidence supports the Examiner's finding that Matsuura's soybean extract inherently contains trypsin inhibitory activity.

SUMMARY

Because our decision relies on additional evidence that was not set forth by the Examiner, we designate our decision as a new ground of rejection under 37 C.F.R. § 41.50(b).

This decision contains new grounds of rejection pursuant to 37 C.F.R. § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 C.F.R. § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 C.F.R. § 41.50(b) also provides that the Appellants, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

(1) Reopen prosecution. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the Examiner, in which event the proceeding will be remanded to the Examiner. . . .

(2) Request rehearing. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

§ 41.50(b)

enc: Van der Ven et al., *Inactivation of Soybean Trypsin Inhibitors and Lipoxygenase by High-Pressure Processing*, 53 J. AGRIC. FOOD CHEM. 1087-1092 (2005).
Kwok et al., *Optimizing Conditions for Thermal Processes of Soy Milk*, 50 J. AGRIC. FOOD CHEM. 4834-4838 (2002).

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